

At page 131, line 2, after "Hum. Genet.," please delete "____:_____" and insert in place thereof --87(4):489-494--.

At page 140, line 11, after "Genomics," please delete "____:_____" and insert in place thereof --11(3):565-572--.

At page 144, line 25, after "Genomics," please delete "____:_____" and insert in place thereof --11(4):997-1006--.

At page 145, line 11, after "Genomics," please delete "____:_____" and insert in place thereof --11(3):565-572--.

IN THE CLAIMS:

Kindly cancel claims 1-20 without prejudice or disclaimer.

Kindly add new claims 48-94 follows:

--48. A method of staining target chromosomal material comprising:

(a) providing at least one labeled nucleic acid probe having a complexity greater than about 40 kb, which labeled nucleic acid probe comprises fragments which are substantially complementary to unique nucleic acid segments within the chromosomal material for which detection is desired, and providing blocking nucleic acid that comprises fragments which are substantially complementary to repetitive segments in the labeled nucleic acid; and

(b) employing said labeled nucleic acid probe, blocking nucleic acid, and chromosomal DNA in in situ hybridization so that labeled repetitive segments, if present,

are substantially blocked from binding to the chromosomal DNA, while hybridization of unique segments within the labeled nucleic acid probe to the chromosomal DNA is allowed, wherein blocking of the labeled repetitive segments is sufficient to permit detection of hybridized labeled nucleic acid containing unique segments, and wherein the chromosomal DNA is present in a morphologically identifiable chromosome or cell nucleus during the in situ hybridization.

49. The method of claim 48, wherein the chromosomal DNA is present in a morphologically identifiable chromosome.

50. The method of claim 48, wherein the chromosomal DNA is present in a cell nucleus during the in situ hybridization.

51. The method of claim 48, wherein the chromosomal material is from a fetal cell.

52. The method of claim 49, further comprising the step of separating the fetal cell from maternal blood.

53. The method of claim 48, wherein the labeled nucleic acid probe comprises heterogeneous mixtures of labeled nucleic acid fragments, wherein the nucleic

acid fragments are substantially complementary to sites on the targeted chromosomal material and are substantially free of nucleic acid sequences having a hybridization capacity to sites on chromosomal material that is not targeted.

54. The method of claim 48, wherein the labeled nucleic acid probe comprises fragments which are designed to allow detection of extra or missing chromosomes.

55. The method of claim 48, wherein the labeled nucleic acid probe comprises fragments which are designed to allow detection of extra or missing portions of a chromosome.

56. The method of claim 48, wherein the labeled nucleic acid probe comprises fragments which are designed to allow detection of chromosomal rearrangement.

57. The method of claim 56, wherein the chromosomal rearrangement is an inversion.

58. The method of claim 56, wherein the chromosomal rearrangement is an insertion.

59. The method of claim 56, wherein the chromosomal rearrangement is a translocation.

60. The method of claim 56, wherein the chromosomal rearrangement is an amplification.

61. The method of claim 56, wherein the chromosomal rearrangement is a deletion.

62. The method of claim 48, wherein the target chromosomal material is present in an interphase cell nucleus.

63. The method of claim 62, wherein the labeled nucleic acid has a complexity of between about 40 kb and 100 kb.

64. The method of claim 62, wherein the labeled nucleic acid has a complexity between about 50 kb and 400 kb.

65. The method of claim 48, wherein the labeled nucleic acid comprises fragments complementary to the total genomic complement of chromosomes.

66. The method of claim 48, wherein the labeled nucleic acid comprises fragments complementary to a single chromosome.

67. The method of claim 48, wherein the labeled nucleic acid comprises fragments complementary to a subset of chromosomes.

68. The method of claim 48, wherein the labeled nucleic acid comprises fragments complementary to a subregion of a single chromosome.

69. The method of claim 48, wherein the labeled nucleic acid is designed to allow detection of cancer.

70. The method of claim 48, wherein the labeled nucleic acid is designed to allow detection of retinoblastoma.

71. The method of claim 48, further comprising removing from the labeled nucleic acid fragments which are substantially complementary to repetitive segments within the target chromosomal material.

72. A method of staining target chromosomal material comprising:

sl
H17

(a) providing at least one labeled nucleic acid probe having a complexity greater than about 40 kb, which labeled nucleic acid probe comprises fragments which are substantially complementary to unique nucleic acid segments within the chromosomal material for which detection is desired, wherein fragments substantially complementary to repetitive segments in the target chromosomal material have been removed from the labeled nucleic acid probe; and

(b) employing said labeled nucleic acid probe and chromosomal DNA in in situ hybridization so that hybridization of unique segments within the labeled nucleic acid probe to the chromosomal DNA is allowed, and hybridized labeled nucleic acid containing unique segments are detected, and wherein the chromosomal DNA is present in a morphologically identifiable chromosome or cell nucleus during the in situ hybridization.

G
Cont.

73. The method of claim 72, further comprising providing blocking nucleic acid that comprises fragments which are substantially complementary to repetitive segments in the labeled nucleic acid probe and employing said blocking nucleic acid in in situ hybridization so that labeled repetitive segments, if present, are substantially blocked from binding to the chromosomal DNA.

74. The method of claim 72, wherein the chromosomal DNA is present in a morphologically identifiable chromosome.

75. The method of claim 72, wherein the chromosomal DNA is present in a cell nucleus during the in situ hybridization.

76. The method of claim 72, wherein the chromosomal material is from a fetal cell.

77. The method of claim 76, further comprising the step of separating the fetal cell from maternal blood.

78. The method of claim 72, wherein the labeled nucleic acid probe comprises heterogeneous mixtures of labeled nucleic acid fragments, wherein the nucleic acid fragments are substantially complementary to sites on the targeted chromosomal material and are substantially free of nucleic acid sequences having a hybridization capacity to sites on chromosomal material that is not targeted.

79. The method of claim 72, wherein the labeled nucleic acid probe comprises fragments which are designed to allow detection of extra or missing chromosomes.

80. The method of claim 72, wherein the labeled nucleic acid probe comprises fragments which are designed to allow detection of extra or missing portions of a chromosome.

81. The method of claim 72, wherein the labeled nucleic acid probe comprises fragments which are designed to allow detection of chromosomal rearrangement.

82. The method of claim 81, wherein the chromosomal rearrangement is an inversion.

83. The method of claim 81, wherein the chromosomal rearrangement is an insertion.

84. The method of claim 81, wherein the chromosomal rearrangement is a translocation.

85. The method of claim 81, wherein the chromosomal rearrangement is an amplification.

86. The method of claim 81, wherein the chromosomal rearrangement is a deletion.

87. The method of claim 72, wherein the target chromosomal material is an interphase chromosome.

I 88. The method of claim ⁷²~~87~~, wherein the labeled nucleic acid has a complexity of between about 40 kb and 100 kb.

I 89. The method of claim ⁷²~~87~~, wherein the labeled nucleic acid has a complexity between about 50 kb and 100 kb.

90. The method of claim 72, wherein the labeled nucleic acid comprises fragments complementary to the total genomic complement of chromosomes.

91. The method of claim 72, wherein the labeled nucleic acid comprises fragments complementary to a single chromosome.

G Cont. 92. The method of claim 72, wherein the labeled nucleic acid comprises fragments complementary to a subregion of a single chromosome.

93. The method of claim 72, wherein the labeled nucleic acid is designed to allow detection of cancer.